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Redx’s strange insolvency triggers Imbruvica follow-on buzz

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Loxo’s outright acquisition of Redx Pharma’s BTK inhibitor programme yesterday was a sobering lesson in UK biotech investing: Redx had been put into administration when a local authority called in a relatively insignificant loan in May.

But beyond the odd aspects of the deal the message is that BTK inhibition is still interesting, and Loxo must think that, even at $40m for a preclinical asset, it has picked up a bargain. One of the reasons might be that several BTK-targeting assets are now being studied beyond oncology, in uses such as graft-versus-host, lupus, rheumatoid arthritis and even multiple sclerosis (see table below).

Of course, it is too early to tell in which direction the Redx programme, in which the lead is RXC005, will go. When the recently listed UK biotech’s chief executive spoke to *EP Vantage* two years ago the focus was cancer and Imbruvica-resistant patients (*Interview – Redx Pharma banks on déjà vu, June 26, 2015*).

It was Imbruvica, of course, that had started off the craze when it became the first drug to show the potential of BTK inhibition, a mechanism that had been studied for decades. Its originator, Pharmacyclics, was bought by Abbvie for $21bn, and *EvaluatePharma’s* sellside forecasts are for 2022 sales to hit $7.5bn.

While most of these revenues will come from haematological malignancies, Imbruvica’s post-oncology focus centres on graft-versus-host disease, a use in which it is awaiting approval.

Beyond Imbruvica, perhaps the broadest phase III programme of any BTK inhibitor concerns Astrazeneca and Acerta Pharma’s acalabrutinib; while this, like RXC005, initially targets Imbruvica-resistant patients, it has also been studied in rheumatoid arthritis.

Even starker examples of looking beyond oncology are clinical BTK assets owned by Bristol-Myers Squibb, Merck KGaA, Lilly, Takeda, Roche, Biogen and Acea, which all have rheumatoid arthritis as their leading indication. Lupus is another increasingly popular indication, while evobrutinib and BIIB068 are in early trials for multiple sclerosis.

Selected BTK inhibitor projects		
Project	**Company**	**Indications**
Marketed		
Imbruvica	AbbVie/J&J	Launched for CLL & other haematological malignancies; awaiting registration for GvHD
Phase III		
Acalabrutinib	Astrazeneca/Acerta	Haem & solid tumours, rheumatoid arthritis (phase II)
BGB-3111	Beigene	Haem malignancies
Phase II		
SNS-062	Sunesis	Haem malignancies
BMS-986142	Bristol-Myers Squibb	Rheumatoid arthritis
Evobrutinib	Merck KGaA	Rheumatoid arthritis, systemic lupus erythematosus, multiple sclerosis
Poseltinib	Lilly/Hanmi	Rheumatoid arthritis
Tirabrutinib	Gilead/Ono	Haem malignancies, Sjögren's syndrome (phase II), rheumatoid arthritis (phase I)
M7583	Merck KGaA	Haem malignancies
RG7845	Roche	Rheumatoid arthritis, systemic lupus erythematosus
PRN1008	Principia Biopharma	Pemphigus vulgaris
Phase I		
ARQ 531	Arqule	Haem malignancies
TAK-020	Takeda/Ligand	Rheumatoid arthritis
BIIB068	Biogen	Systemic lupus erythematosus, multiple sclerosis
AC0058	Acea Biosciences	Rheumatoid arthritis, systemic lupus erythematosus
Preclinical		
RXC005/LOXO-305	Redx/Loxo	Oncology
ABBV-599	Abbvie	Rheumatoid arthritis; BTK & Jak inhibitor
AS-871	Carna Biosciences	Oncology
LSK9985	LSK Biopharma	Rheumatoid arthritis; BTK & Jak3 inhibitor
PRN2246	Principia Biopharma	CNS applications
BTKwt	X-Rx	Immunosuppressant
Source: EvaluatePharma, Clinicaltrials.gov.		

The breadth of the proposed uses has a precedent. BTK is reckoned to play a role in B-cell maturation, and multiple sclerosis is thought to have B-cell involvement – witness the development by Roche of Ocrevus, which hits CD20, a leukaemia target, and is now seen as one of the most important new multiple sclerosis drugs.

Of course, for RXC005, which Loxo now calls LOXO-305, it is still early days. But Redx’s unfortunate investors might well ask themselves whether the asset was let go for a song.

This might especially apply seeing as Astra paid $2.5bn for a majority stake in Acerta and acalabrutinib, while Lilly got poseltinib from Hanmi for $50m up front (*Ash – Early data for next generation of Imbruvica's challengers, December 6, 2016*). Still, RXC005 is only preclinical, and had it not been for a bizarre chain of events it might not even have been up for licensing out.

In a barely believable scenario Redx declared itself insolvent after Liverpool City Council, a UK local authority, called in a five-year-old loan of just £2.0m ($2.6m), and its stock was suspended on May 24. The group's administrators shopped its assets around, and found in Loxo a keen buyer of BTK; the insolvency explains why the asset was sold outright, with no royalty or milestone element.

With $40m of ready cash in the bank it seems likely that Redx can now settle the loan and exit administration. It will be interesting to see where its stock resumes trading – remarkably, $40m is not far off the group's market capitalisation at the point it was suspended from Aim.

If Redx exits administration its immediate future will rest on inhibitors of IDO and the Hedgehog pathway. The question for investors will be whether these are viable or whether Redx's valuation reflected just the BTK inhibitor for a reason.